Getting it right: WHO guidance to diagnose correctly 90% of people living with HIV

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World Health Organization
Aims of the new WHO HTS guidelines

- Addressing the testing **gap**
- Getting testing out into **communities**
- Supporting better **linkage**
- Better focus and appropriate **targeting**
- Improving **quality** to prevent misdiagnosis
HIV testing quality and misdiagnosis

Studies (N=44) identified in a literature review, reporting factors related to misdiagnosis

<table>
<thead>
<tr>
<th>Category</th>
<th>#</th>
<th>%</th>
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<tbody>
<tr>
<td>Clerical/technical errors (e.g. mis-labelling, poor recordkeeping, clerical mistakes)</td>
<td>14</td>
<td>32%</td>
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<tr>
<td>User error (e.g. errors performing RDT or interpreting results, misapplication of buffer, inaccurate reading time and other human errors)</td>
<td>11</td>
<td>48%</td>
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<tr>
<td>Cross-reactivity (e.g. antibodies from inter-current infection, environmental exposure to test components, HIV subtype, or late-stage AIDS)</td>
<td>8</td>
<td>18%</td>
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<td>Incorrect / suboptimal testing strategy or algorithm (e.g. tiebreaker testing strategy)</td>
<td>22</td>
<td>50%</td>
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<td>Poor management and supervision (work load stress, staff shortages, lack of training, poor adherence to testing strategy or testing algorithm, substandard operating procedures, testing in window period)</td>
<td>20</td>
<td>45%</td>
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National testing policies aligned with WHO recommendations
48 countries

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<th>Category</th>
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| Clerical/technical errors         | 17%
| User error                        | 16%
| Cross-reactivity                  | 15%
| Incorrect / suboptimal testing strategy or algorithm | 15%
| Poor management and supervision   | 15%

Review identified reports of misclassification range from 2.6% to 10.3%\(^1,2\)

Assuring quality of diagnostics

Key points

1. Chose a **testing strategy** (high or low prevalence)
2. Select products and validate the **testing algorithm**
3. Ensure **post-market surveillance** of products used
HIV testing definitions

- A **testing strategy** describes an approach for a specific testing purpose considering presumed HIV prevalence in the **population being tested**.

- A **testing algorithm** describes the products (brands) of HIV assays to be used within a given HIV testing strategy.

- **Positive predicative value** determines the probability that the test result obtained reflects the true result.

- An **assay** is a procedure for measuring the presence of a given analyte, e.g. antibodies to HIV-1/2.
Diagnosis - high prevalence (above 5%)

- **A1-** = negative
- **A1+; A2+** = positive
- **A1+; A2-; A3-** = negative
- **A1+; A2-; A3+** = inconclusive
Diagnosis - low prevalence (below 5%)

- A1- = negative
- A1+; A2- = negative or inconclusive
- A1+; A2+; A3+ = positive
- A1+; A2+; A3- = inconclusive
Re-testing recommendations

- Retesting means
  - Different specimen, same testing algorithm, different testing site
  - Significant limitations when on ART

- Individuals with **HIV-inconclusive** status should be retested after 14 days
  - To rule in or rule out seroconversion (static vs. evolving results)
  - To rule out operator error, test device error, transcription errors

- **Newly diagnosed HIV-positive** individuals should be retested prior to care and/or treatment
Validation of testing algorithms

- Choose:
  - 6-10 assays from list of prequalified assays

- Conduct:
  - Validation study to identify best combination of assays

- Select:
  - One A1 (and back-up) with superior sensitivity
  - One each for A2 and A3 with superior specificity
Limitations of certain diagnostics

- **Inadequate internal QC**
  - Most RDTs don't control for specimen addition

- **Assays for detection of HIV-2**
  - Up to 57% cross-reactivity observed for "discriminatory" HIV-1/HIV-2 assays

- **4th generation (Ag/Ab) assays**
  - Designed for use as A1
  - Current products have limitations for detecting acute infection but good sensitivity for established infection
How to assure quality of HIV testing

- **Assessment**
  - EQA, supervisory visits
- **Process control**
  - QC, including storage
- **Recordkeeping and documentation**
- **Personnel**
  - Training, support
Contact us

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